General

Guideline Title

Clinical practice guidelines for hypothyroidism in adults: cosponsored by the American Association of Clinical Endocrinologists and the American Thyroid Association.

Bibliographic Source(s)

Garber JR, Cobin RH, Gharib H, Hennessey JV, Klein I, Mechanick JI, Pessah-Pollack R, Singer PA, Woeber KA, American Association of Clinical Endocrinologists and American Thyroid Association. Clinical practice guidelines for hypothyroidism in adults: cosponsored by the American Association of Clinical Endocrinologists and the American Thyroid Association. Endocr Pract. 2012 Nov-Dec;18(6):988-1028. [311 references] PubMed

Guideline Status

This is the current release of this guideline.

This guideline updates previous versions:

AACE Thyroid Task Force. American Association of Clinical Endocrinologists medical guidelines for clinical practice for the evaluation and treatment of hyperthyroidism and hypothyroidism. Endocr Pract. 2002 Nov-Dec;8(6):457-69. [46 references]

Singer PA, Cooper DS, Levy EG, Ladenson PW, Braverman LE, Daniels G, Greenspan FS, McDougall IR, Nikolai TF. Treatment guidelines for patients with hyperthyroidism and hypothyroidism. Standards of Care Committee, American Thyroid Association. JAMA. 1995 Mar 8;273(10):808-12. [13 references]

Recommendations

Major Recommendations

The levels of evidence (1–4) and the recommendation grades (A–D) are defined at the end of the "Major Recommendations" field.

Questions and Guideline Recommendations

The recommendations are evidence-based (Grades A, B, and C) or based on expert opinion because of a lack of conclusive clinical evidence (Grade D). The "best evidence" rating level (BEL), which corresponds to the best conclusive evidence found, accompanies the recommendation grade.

Note: When referring to therapy and therapeutic preparations in the recommendations and elsewhere, L-thyroxine and L-triiodothyronine are generally used instead of their respective hormonal equivalents, T_4 and T_3.

When Should Anti-Thyroid Antibodies be Measured?

Recommendation 1: Anti-thyroid peroxidase antibody (TPOAb) measurements should be considered when evaluating patients with subclinical hypothyroidism (Grade B; BEL 1).

Recommendation 2: TPOAb measurement should be considered in order to identify autoimmune thyroiditis when nodular thyroid disease is suspected to be due to autoimmune thyroid disease (Grade D; BEL 4).

Recommendation 3: TPOAb measurement should be considered when evaluating patients with recurrent miscarriage, with or without infertility (Grade A; BEL 2).

Recommendation 4: Measurement of serum thyrotropin (TSH) receptor antibodies (TSHRAbs) using a sensitive assay should be considered in hypothyroid pregnant patients with a history of Graves' disease who were treated with radioactive iodine or thyroidectomy prior to pregnancy. This should be initially done either at 20–26 weeks of gestation or during the first trimester and if they are elevated again at 20–26 weeks of gestation (Grade A; BEL 2).

What is the Role of Clinical Scoring Systems in the Diagnosis of Patients With Hypothyroidism?

Recommendation 5: Clinical scoring systems should not be used to diagnose hypothyroidism (Grade A; BEL 1).

What is the Role of Diagnostic Tests Apart From Serum Thyroid Hormone Levels and TSH in the Evaluation of Patients With Hypothyroidism?

Recommendation 6: Tests such as clinical assessment of reflex relaxation time, cholesterol, and muscle enzymes should not be used to diagnose hypothyroidism (Grade B; BEL 2).

What Are the Preferred Thyroid Hormone Measurements in Addition to TSH in the Assessment of Patient With Hypothyroidism?

Recommendation 7: Apart from pregnancy, assessment of serum free thyroxine (T_4) should be done instead of total T_4 in the evaluation of hypothyroidism. An assessment of serum free T_4 includes a free T_4 index or free T_4 estimate and direct immunoassay of free T_4 without physical separation using anti-T_4 antibody (Grade A; BEL 1).

Recommendation 8: Assessment of serum free T_4, in addition to TSH, should be considered when monitoring L-thyroxine therapy (Grade B; BEL 1).

Recommendation 9: In pregnancy, the measurement of total T_4 or a free T_4 index, in addition to TSH, should be done to assess thyroid status. Because of the wide variation in the results of different free T_4 assays, direct immunoassay measurement of free T_4 should only be employed when method-specific and trimester-specific reference ranges for serum free T_4 are available (Grade B; BEL 2).

Recommendation 10: Serum total T_3 or assessment of serum free T_3 should not be done to diagnose hypothyroidism (Grade A; BEL 2).

Recommendation 11: TSH measurements in hospitalized patients should be done only if there is an index of suspicion for thyroid dysfunction (Grade A; BEL 2).

Recommendation 12: In patients with central hypothyroidism, assessment of free T_4 or free T_4 index, not TSH, should be done to diagnose and guide treatment of hypothyroidism (Grade A; BEL 1).

When Should TSH Levels Be Measured in Patients Being Treated For hypothyroidism?

Recommendation 13: Patients being treated for established hypothyroidism should have serum TSH measurements done at 4–8 weeks after initiating treatment or after a change in dose. Once an adequate replacement dose has been determined, periodic TSH measurements should be done after 6 months and then at 12-month intervals, or more frequently if the clinical situation dictates otherwise (Grade B; BEL 2).

What Should Be Considered the Upper Limit of the Normal Range of TSH Values?

Recommendation 14.1: The reference range of a given laboratory should determine the upper limit of normal for a third generation TSH assay. The normal TSH reference range changes with age. If an age-based upper limit of normal for a third generation TSH assay is not available in an iodine sufficient area, an upper limit of normal of 4.12 should be considered (Grade A; BEL 1).

Recommendation 14.2: In pregnancy, the upper limit of the normal range should be based on trimester-specific ranges for that laboratory. If trimester-specific reference ranges for TSH are not available in the laboratory, the following upper normal reference ranges are recommended: first

trimester, 2.5 mIU/L; second trimester, 3.0 mIU/L; third trimester, 3.5 mIU/L (Grade B; BEL 2).

Which Patients With TSH levels Above a Given Laboratory's Reference Range Should Be Considered For Treatment With L-Thyroxine?

Recommendation 15: Patients whose serum TSH levels exceed 10 mIU/L are at increased risk for heart failure and cardiovascular mortality, and should be considered for treatment with L-thyroxine (Grade B; BEL 1).

Recommendation 16: Treatment based on individual factors for patients with TSH levels between the upper limit of a given laboratory's reference range and 10 mIU/L should be considered particularly if patients have symptoms suggestive of hypothyroidism, positive TPOAb or evidence of atherosclerotic cardiovascular disease, heart failure, or associated risk factors for these diseases (Grade B; BEL 1).

In Patients With Hypothyroidism Being Treated With L-Thyroxine, What Should the Target TSH Range Be?

Recommendation 17: In patients with hypothyroidism who are not pregnant, the target range should be the normal range of a third generation TSH assay. If an upper limit of normal for a third generation TSH assay is not available, in iodine sufficient areas an upper limit of normal of 4.12 mIU/L should be considered and if a lower limit of normal is not available, 0.45 mIU/L should be considered (Grade B; BEL 2).

In Patients With Hypothyroidism Being Treated With L-Thyroxine Who Are Pregnant, What Should the Target TSH Ranges Be?

Recommendation 18: In patients with hypothyroidism who are pregnant, the target range for TSH should be based on trimester-specific ranges for that laboratory. If trimester-specific reference ranges are not available in the laboratory, the following upper-normal reference ranges are recommended: first trimester, 2.5 mIU/L; second trimester, 3.0 mIU/L; and third trimester, 3.5 mIU/L (Grade C; BEL 2).

Which Patients With Normal Serum TSH Levels Should Be Considered For Treatment With L-Thyroxine?

Recommendation 19.1: Treatment with L-thyroxine should be considered in women of childbearing age with serum TSH levels between 2.5 mIU/L and the upper limit of normal for a given laboratory's reference range if they are in the first trimester of pregnancy or planning a pregnancy including assisted reproduction in the immediate future. Treatment with L-thyroxine should be considered in women in the second trimester of pregnancy with serum TSH levels between 3.0 mIU/L and the upper limit of normal for a given laboratory's reference range, and in women in the third trimester of pregnancy with serum TSH levels between 3.5 mIU/L and the upper limit of normal for a given laboratory's reference range (Grade B; BEL 2).

Recommendation 19.2: Treatment with L-thyroxine should be considered in women of childbearing age with normal serum TSH levels when they are pregnant or planning a pregnancy, including assisted reproduction in the immediate future, if they have or have had positive levels of serum TPOAb, particularly when there is a history of miscarriage or past history of hypothyroidism (Grade B; BEL 2).

Recommendation 19.3: Women of childbearing age who are pregnant or planning a pregnancy, including assisted reproduction in the immediate future, should be treated with L-thyroxine if they have or have had positive levels of serum TPOAb and their TSH is greater than 2.5 mIU/L (Grade B; BEL 2).

Recommendation 19.4: Women with positive levels of serum TPOAb or with a TSH greater than 2.5 mIU/L who are not being treated with L-thyroxine should be monitored every 4 weeks in the first 20 weeks of pregnancy for the development of hypothyroidism (Grade B; BEL 2).

Who, Among Patients Who Are Pregnant, or Planning Pregnancy, or With Other Characteristics, Should Be Screened For Hypothyroidism?

Recommendation 20.1.1: Universal screening is not recommended for patients who are pregnant or are planning pregnancy, including assisted reproduction (Grade B; BEL 1).

Recommendation 20.1.2: "Aggressive case finding" rather than universal screening, should be considered for patients who are planning pregnancy (Grade C; BEL 2).

Recommendation 20.2: Screening for hypothyroidism should be considered in patients over the age of 60 (Grade B; BEL 1).

Recommendation 21: "Aggressive case finding," should be considered in those at increased risk for hypothyroidism (Grade B; BEL 2).

How Should Patients With Hypothyroidism Be Treated and Monitored?

Recommendation 22.1: Patients with hypothyroidism should be treated with L-thyroxine monotherapy (Grade A; BEL 1).

Recommendation 22.2: The evidence does not support using L-thyroxine and L-triiodothyronine combinations to treat hypothyroidism (Grade B; BEL 1).

Recommendation 22.3: L-thyroxine and L-triiodothyronine combinations should not be administered to pregnant women or those planning pregnancy (Grade B; BEL 3).

Recommendation 22.4: There is no evidence to support using desiccated thyroid hormone in preference to L-thyroxine monotherapy in the treatment of hypothyroidism and therefore desiccated thyroid hormone should not be used for the treatment of hypothyroidism (Grade D; BEL 4).

Recommendation 22.5: 3,5,3'-triiodothyroacetic acid (TRIAC; tiratricol) should not be used to treat primary and central hypothyroidism due to suggestions of harm in the literature (Grade C; BEL 3).

Recommendation 22.6: Patients resuming L-thyroxine therapy after interruption (less than 6 weeks) and without an intercurrent cardiac event or marked weight loss may resume their previously employed full replacement doses (Grade D; BEL 4).

Recommendation 22.7.1: When initiating therapy in young healthy adults with overt hypothyroidism, beginning treatment with full replacement doses should be considered (Grade B; BEL 2).

Recommendation 22.7.2: When initiating therapy in patients older than 50–60 years with overt hypothyroidism, without evidence of coronary heart disease, an L-thyroxine dose of 50 μg daily should be considered (Grade D; BEL 4).

Recommendation 22.8: In patients with subclinical hypothyroidism initial L-thyroxine dosing is generally lower than what is required in the treatment of overt hypothyroidism. A daily dose of 25–75 μg should be considered, depending on the degree of TSH elevation. Further adjustments should be guided by clinical response and follow-up laboratory determinations including TSH values (Grade B; BEL 2).

Recommendation 22.9: Treatment with glucocorticoids in patients with combined adrenal insufficiency and hypothyroidism should precede treatment with L-thyroxine (Grade B; BEL 2).

Recommendation 23: L-thyroxine should be taken with water consistently 30–60 minutes before breakfast or at bedtime 4 hours after the last meal. It should be stored properly per product insert and not taken with substances or medications that interfere with its absorption (Grade B; BEL 2).

Recommendation 24: In patients with central hypothyroidism, assessments of serum free T_4 should guide therapy and targeted to exceed the midnormal range value for the assay being used (Grade B; BEL 3).

Recommendation 25.1: In patients with hypothyroidism being treated with L-thyroxine who are pregnant, serum TSH should be promptly measured after conception and L-thyroxine dosage adjusted, with a goal TSH of less than 2.5 mIU/L during the first trimester (Grade B, BEL 2).

Recommendation 25.2: In patients with hypothyroidism being treated with L-thyroxine who are pregnant, the goal TSH during the second trimester should be less than 3 mIU/L and during the third trimester should be less than 3.5 mIU/L (Grade C; BEL 2).

Recommendation 25.3: Maternal serum TSH (and total T_4) should be monitored every 4 weeks during the first half of pregnancy and at least once between 26 and 32 weeks gestation and L-thyroxine dosages adjusted as indicated (Grade B; BEL 2).

Recommendation 26: In patients receiving L-thyroxine treatment for hypothyroidism, serum TSH should be remeasured within 4–8 weeks of initiation of treatment with drugs that decrease the bioavailability or alter the metabolic disposition of the L-thyroxine dose (Grade A; BEL 1).

Recommendation 27: Apart from pregnant patients being treated with L-thyroxine for hypothyroidism, the evidence does not support targeting specific TSH values within the normal reference range (Grade B; BEL 2).

When Should Endocrinologists Be Involved in the Care of Patients With Hypothyroidism?

Recommendation 28: Physicians who are not endocrinologists, but who are familiar with the diagnosis and treatment of hypothyroidism *should be* able to care for most patients with primary hypothyroidism. However, patients with hypothyroidism who fall into the following categories should be seen in consultation with an endocrinologist. These categories are (i) children and infants, (ii) patients in whom it is difficult to render and maintain a euthyroid state, (iii) pregnancy, (iv) women planning conception, (v) cardiac disease, (vi) presence of goiter, nodule, or other structural changes in the thyroid gland, (vii) presence of other endocrine disease such as adrenal and pituitary disorders, (viii) unusual constellation of thyroid function test results, and (ix) unusual causes of hypothyroidism such as those induced by agents that interfere with absorption of L-thyroxine impact thyroid gland hormone production or secretion, affect the hypothalamic-pituitary-thyroid axis (directly or indirectly), increase clearance, or peripherally impact metabolism (Grade C; BEL 3).

Which Patients Should Not Be Treated With Thyroid Hormone?

Recommendation 29: Thyroid hormones should not be used to treat symptoms suggestive of hypothyroidism without biochemical confirmation of the diagnosis (Grade B; BEL 2).

Recommendation 30: Thyroid hormones should not be used to treat obesity in euthyroid patients (Grade A; BEL 2).

Recommendation 31: There is insufficient evidence to support using thyroid hormones to treat depression in euthyroid patients (Grade B; BEL 2).

What is the Role of Iodine Supplementation, Dietary Supplements, and Nutraceuticals in the Treatment of Hypothyroidism?

Recommendation 32.1: Iodine supplementation, including kelp or other iodine-containing functional foods, should not be used in the management of hypothyroidism in iodine-sufficient areas (Grade C; BEL 3).

Recommendation 32.2: Iodine supplementation in the form of kelp or other seaweed-based products should not be used to treat iodine deficiency in pregnant women (Grade D; BEL 4).

Recommendation 33: Selenium should not be used to prevent or treat hypothyroidism (Grade B; BEL 2).

Recommendation 34: Patients taking dietary supplements and nutraceuticals for hypothyroidism should be advised that commercially available thyroid-enhancing products are not a remedy for hypothyroidism and should be counseled about the potential side effects of various preparations particularly those containing iodine or sympathomimetic amines as well as those marked as "thyroid support" since they could be adulterated with L-thyroxine or L-triiodothyronine (Grade D; BEL 4).

Definitions:

Levels of Scientific Substantiation in Evidence-based Medicine*

Level	Description	Comments
1	Prospective, randomized, controlled trials—large	Data are derived from a substantial number of trials with adequate statistical power involving a substantial number of outcome data subjects.
		Large meta-analyses using raw or pooled data or incorporating quality ratings
		Well-controlled trial at one or more centers
		Consistent pattern of findings in the population for which the recommendation is made (generalizable data).
		Compelling nonexperimental, clinically obvious, evidence (e.g., thyroid hormone treatment for myxedema coma), "all-or-none" indication
2	Prospective controlled trials with or without randomization—limited body of outcome data	Limited number of trials, small population sites in trials
		Well-conducted single-arm prospective cohort study
		Limited but well-conducted meta-analyses
		Inconsistent findings or results not representative for the target population
		Well-conducted case-controlled study
3	Other experimental outcome data and nonexperimental data	Nonrandomized, controlled trials
		Uncontrolled or poorly controlled trials
		Any randomized clinical trial with one or more major or three or more minor methodological flaws
		Retrospective or observational data
		Case reports or case series
		Conflicting data with weight of evidence unable to support a final recommendation
4	Expert opinion	Inadequate data for inclusion in level 1, 2, or 3; necessitates an expert panel's

Level	Description	Comments
		synthesis of the literature and a consensus Experience based Theory driven

*Levels 1, 2, and 3 represent a given level of scientific substantiation or proof. Level 4 or Grade D represents unproven claims. It is the "best evidence" based on the individual ratings of clinical reports that contributes to a final grade recommendation.

2010 American Association of Clinical Endocrinologists (AACE) Protocol for Production of Clinical Practice Guidelines—Step III: Grading of Recommendations; How Different Evidence Levels Can be Mapped to the Same Recommendation Grade

Best Evidence Level	Subjective Factor Impact	Two-thirds Consensus	Mapping[a]	Recommendation Grade
1	None	Yes	Direct	A
2	Positive	Yes	Adjust up	A
2	None	Yes	Direct	B
1	Negative	Yes	Adjust down	B
3	Positive	Yes	Adjust up	B
3	None	Yes	Direct	C
2	Negative	Yes	Adjust down	C
4	Positive	Yes	Adjust up	C
4	None	Yes	Direct	D
3	Negative	Yes	Adjust down	D
1, 2, 3, 4	N/A	No	Adjust down	D

Adopted by the American Association of Clinical Endocrinologists (AACE) and the American Thyroid Association (ATA) for the Hypothyroidism Clinical Practice Guidelines (CPG).

[a] Starting with the left column, best evidence levels (BELs), subjective factors, and consensus map to recommendation grades in the right column. When subjective factors have little or no impact ("none"), then the BEL is directly mapped to recommendation grades. When subjective factors have a strong impact, then recommendation grades may be adjusted up ("positive" impact) or down ("negative" impact). If a two-thirds consensus cannot be reached, then the recommendation grade is D.

N/A, not applicable (regardless of the presence or absence of strong subjective factors, the absence of a two-thirds consensus mandates a recommendation grade D).

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Hypothyroidism, overt or subclinical

Note: Subclinical hypothyroidism is characterized by a serum thyrotropin (TSH) above the upper reference limit in combination with a normal free thyroxine (T_4). This designation is only applicable when thyroid function has been stable for weeks or more, the hypothalamic-pituitary-thyroid axis

is normal, and there is no recent or ongoing severe illness. An elevated TSH, usually above 10 mIU/L, in combination with a subnormal free T_4 characterizes overt hypothyroidism.

Guideline Category

Diagnosis

Evaluation

Management

Treatment

Clinical Specialty

Endocrinology

Family Practice

Internal Medicine

Obstetrics and Gynecology

Intended Users

Physicians

Guideline Objective(s)

To present evidence-based clinical guidelines for the clinical management of hypothyroidism in ambulatory patients

Target Population

Ambulatory patients with overt or subclinical hypothyroidism

Interventions and Practices Considered

Diagnosis/Evaluation

1. Anti-thyroid peroxidase antibody (TPOAb) measurements
2. Measurement of serum thyrotropin (TSH) using a sensitive assay
3. Assessment of serum free thyroxine (T_4)
4. Screening for hypothyroidism in patients over the age of 60

Treatment/Management

1. Periodic TSH measurements
2. L-thyroxine

Major Outcomes Considered

- Sensitivity of thyroid-stimulating hormone (TSH) assays and other laboratory tests for diagnosing hypothyroidism
- Morbidity due to subclinical hypothyroidism

- Adverse effects of treatments for hypothyroidism

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

The process was begun by developing an outline for reviewing the principal clinical aspects of hypothyroidism. Computerized and manual searching of the medical literature and various databases, primarily including Medline® and PubMed, was based on specific section titles, thereby avoiding inclusion of unnecessary detail and exclusion of important studies. Searches were performed by authors of respective sections, based on their titles and what they believed were relevant. Articles published since the last guidelines were searched, as well as many articles preceding 2002. Compilation of the bibliography was a continual and dynamic process.

Reviews and high level references were included. Since clinical guidelines are considered largely opinion pieces (Level 4) technically some opinion pieces were included.

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Levels of Scientific Substantiation in Evidence-based Medicine*

Level	Description	Comments
1	Prospective, randomized, controlled trials—large	Data are derived from a substantial number of trials with adequate statistical power involving a substantial number of outcome data subjects.
		Large meta-analyses using raw or pooled data or incorporating quality ratings
		Well-controlled trial at one or more centers
		Consistent pattern of findings in the population for which the recommendation is made (generalizable data).
		Compelling nonexperimental, clinically obvious, evidence (e.g., thyroid hormone treatment for myxedema coma), "all-or-none" indication
2	Prospective controlled trials with or without randomization—limited body of outcome data	Limited number of trials, small population sites in trials
		Well-conducted single-arm prospective cohort study
		Limited but well-conducted meta-analyses
		Inconsistent findings or results not representative for the target population

Level	Description	Comments
		Well-conducted case-controlled study
3	Other experimental outcome data and nonexperimental data	Nonrandomized, controlled trials
		Uncontrolled or poorly controlled trials
		Any randomized clinical trial with one or more major or three or more minor methodological flaws
		Retrospective or observational data
		Case reports or case series
		Conflicting data with weight of evidence unable to support a final recommendation
4	Expert opinion	Inadequate data for inclusion in level 1, 2, or 3; necessitates an expert panel's synthesis of the literature and a consensus
		Experience based
		Theory driven

*Levels 1, 2, and 3 represent a given level of scientific substantiation or proof. Level 4 or Grade D represents unproven claims. It is the "best evidence" based on the individual ratings of clinical reports that contributes to a final grade recommendation.

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review

Description of the Methods Used to Analyze the Evidence

All clinical data that are incorporated in these clinical practice guidelines (CPGs) have been evaluated in terms of levels of scientific substantiation. The detailed methodology for assigning evidence levels (ELs) to the references used in these CPGs has been reported by Mechanick et al. (see the "Rating Scheme for the Strength of Evidence" field). The authors' EL ratings of the references are included in the References section in the original guideline document.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Once the principal clinical aspects of hypothyroidism were defined, questions were formulated with the intent to then develop recommendations that addressed these questions. The grading of recommendations was based on consensus among the authors.

The recommendations are evidence-based (Grades A, B, and C) or based on expert opinion because of a lack of conclusive clinical evidence (Grade D). The "best evidence" rating level (BEL), which corresponds to the best conclusive evidence found, accompanies the recommendation grade. Details regarding the mapping of clinical evidence ratings to these recommendation grades have already been provided (see *Levels of scientific substantiation and recommendation grades [transparency]*). In this clinical practice guideline, a substantial number of recommendations are upgraded or downgraded because the conclusions may not apply in other situations (non-generalizability). For example, what applies to an elderly population with established cardiac disease may not apply to a younger population without cardiac risk factors. Whenever expert opinions resulted in upgrading or downgrading a recommendation, it is explicitly stated after the recommendation.

The four-step approach that the authors used to grade recommendations is summarized in Tables 3, 4, 5, and 6 of the 2010 Standardized

Production of Clinical Practice Guidelines, from which Table 3 in the original guideline document is taken (see the "Availability of Companion Documents" field).

Rating Scheme for the Strength of the Recommendations

2010 American Association of Clinical Endocrinologists (AACE) Protocol for Production of Clinical Practice Guidelines—Step III: Grading of Recommendations; How Different Evidence Levels Can be Mapped to the Same Recommendation Grade

Best Evidence Level	Subjective Factor Impact	Two-thirds Consensus	Mapping[a]	Recommendation Grade
1	None	Yes	Direct	A
2	Positive	Yes	Adjust up	A
2	None	Yes	Direct	B
1	Negative	Yes	Adjust down	B
3	Positive	Yes	Adjust up	B
3	None	Yes	Direct	C
2	Negative	Yes	Adjust down	C
4	Positive	Yes	Adjust up	C
4	None	Yes	Direct	D
3	Negative	Yes	Adjust down	D
1, 2, 3, 4	N/A	No	Adjust down	D

Adopted by the American Association of Clinical Endocrinologists (AACE) and the American Thyroid Association (ATA) for the Hypothyroidism Clinical Practice Guidelines (CPG).

[a] Starting with the left column, best evidence levels (BELs), subjective factors, and consensus map to recommendation grades in the right column. When subjective factors have little or no impact ("none"), then the BEL is directly mapped to recommendation grades. When subjective factors have a strong impact, then recommendation grades may be adjusted up ("positive" impact) or down ("negative" impact). If a two-thirds consensus cannot be reached, then the recommendation grade is D.

N/A, not applicable (regardless of the presence or absence of strong subjective factors, the absence of a two-thirds consensus mandates a recommendation grade D).

Cost Analysis

The guideline developers reviewed published cost analyses.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

The authors, through an a priori methodology and multiple levels of review, have tried to address any shortcomings by discussions with three experts.

The final document was approved by the American Association of Clinical Endocrinologists (AACE) and American Thyroid Association (ATA), and was officially endorsed by the American Association of Diabetes Educators (AADE), American Academy of Otolaryngology—Head and Neck Surgery (AAO-HNS), American College of Endocrinology (ACE), Italian Association of Clinical Endocrinologists (AME), American Society for Metabolic & Bariatric Surgery (ASMBS), The Endocrine Society of Australia (ESA), International Association of Endocrine Surgeons (IAES), Latin American Thyroid Society (LATS), and Ukrainian Association of Endocrine Surgeons (UAES).

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

- Accurate diagnosis and treatment of overt and subclinical hypothyroidism
- Decreased morbidity due to either overt or subclinical hypothyroidism

Potential Harms

- The principal adverse consequences of subtle or frank overtreatment with L-thyroxine are cardiovascular, skeletal, and possibly affective disturbances. The elderly are particularly susceptible to atrial fibrillation, while postmenopausal women, who constitute a substantial portion of those on thyroid hormone, are prone to accelerated bone loss.
- Overt untreated hypothyroidism during pregnancy may adversely affect maternal and fetal outcomes.
- Adverse metabolic effects of iodine supplementation are primarily reported in patients with organification defects (e.g., Hashimoto's thyroiditis) in which severe hypothyroidism ensues and is referred to as "iodide myxedema."

Qualifying Statements

Qualifying Statements

- American Association of Clinical Endocrinologists (AACE) Medical Guidelines for Clinical Practice are systematically developed statements to assist health care professionals in medical decision-making for specific clinical conditions, but are in no way a substitute for a medical professional's independent judgment and should not be considered medical advice. Most of the content herein is based on literature reviews. In areas of uncertainty, professional judgment was applied.
- The American Thyroid Association (ATA) develops Clinical Practice Guidelines to provide guidance and recommendations for particular practice areas concerning thyroid disease, including thyroid cancer. The Guidelines are not inclusive of all proper approaches or methods, or exclusive of others. The Guidelines do not establish a standard of care, and specific outcomes are not guaranteed. Treatment decisions must be made based on the independent judgment of health care providers and each patient's individual circumstances. A guideline is not intended to take the place of physician judgment in diagnosing and treatment of particular patients. It is also not intended to serve as a basis to approve or deny financial coverage for any specific therapeutic or diagnostic modality. The ATA develops guidelines based on the evidence available in the literature and the expert opinion of the task force in the recent timeframe of the publication of the guidelines. Management issues have not been and cannot be comprehensively addressed in randomized trials; therefore, the evidence cannot be comprehensive. Guidelines cannot always account for individual variation among patients. Guidelines cannot be considered inclusive of all proper methods of care or exclusive of other treatments reasonably directed at obtaining the same results. Therefore, the ATA considers adherence to this guideline to be voluntary, with the ultimate determination regarding its application to be made by the treating physician and health care professionals with the full consideration of the individual patient's clinical history and physical status. In addition, the guideline concerns the

therapeutic interventions used in clinical practice and do not pertain to clinical trials. Clinical trials are a separate matter, designed to research new and novel therapies, and the guidelines are not necessarily relevant to their purpose. Guideline development includes an identification of areas for future study and research, indicating the focus for future investigational therapy; based on the findings reviewed and synthesized from the latest literature.

- These guidelines are a document that reflects the current state of the field and are intended to provide a working document for guideline updates since rapid changes in this field are expected in the future. We encourage medical professionals to use this information in conjunction with their best clinical judgment. The presented recommendations may not be appropriate in all situations. Any decision by practitioners to apply these guidelines must be made in light of local resources and individual patient circumstances.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Implementation Tools

Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Living with Illness

Staying Healthy

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

Garber JR, Cobin RH, Gharib H, Hennessey JV, Klein I, Mechanick JI, Pessah-Pollack R, Singer PA, Woeber KA, American Association of Clinical Endocrinologists and American Thyroid Association. Clinical practice guidelines for hypothyroidism in adults: cosponsored by the American Association of Clinical Endocrinologists and the American Thyroid Association. Endocr Pract. 2012 Nov-Dec;18(6):988-1028. [311 references] PubMed

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

1995 Mar 8 (revised 2012 Nov-Dec)

Guideline Developer(s)

American Association of Clinical Endocrinologists - Medical Specialty Society

American Thyroid Association - Professional Association

Source(s) of Funding

American Association of Clinical Endocrinologists (AACE)

Guideline Committee

American Association of Clinical Endocrinologists and American Thyroid Association Taskforce on Hypothyroidism in Adults

Composition of Group That Authored the Guideline

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Financial Disclosures/Conflicts of Interest

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Guideline Endorser(s)

American Academy of Otolaryngology - Head and Neck Surgery - Medical Specialty Society

American Association of Diabetes Educators - Medical Specialty Society

American Association of Endocrine Surgeons - Medical Specialty Society

American College of Endocrinology - Medical Specialty Society

American Society for Metabolic and Bariatric Surgery - Professional Association

Endocrine Society of Australia - Medical Specialty Society

International Association of Endocrine Surgeons - Professional Association

Italian Association of Clinical Endocrinologists - Medical Specialty Society

Korean Thyroid Association - Disease Specific Society

Latin American Thyroid Society - Disease Specific Society

Ukrainian Association of Endocrine Surgeons - Professional Association

Guideline Status

This is the current release of this guideline.

This guideline updates previous versions:

AACE Thyroid Task Force. American Association of Clinical Endocrinologists medical guidelines for clinical practice for the evaluation and treatment of hyperthyroidism and hypothyroidism. Endocr Pract. 2002 Nov-Dec;8(6):457-69. [46 references]

Singer PA, Cooper DS, Levy EG, Ladenson PW, Braverman LE, Daniels G, Greenspan FS, McDougall IR, Nikolai TF. Treatment guidelines for patients with hyperthyroidism and hypothyroidism. Standards of Care Committee, American Thyroid Association. JAMA. 1995 Mar 8;273(10):808-12. [13 references]

Guideline Availability

Electronic copies: Available in Portable Document Format (PDF) from the American Association of Clinical Endocrinologists (AACE) Web site .

Print copies: Available from the American Association of Clinical Endocrinologists (AACE), 245 Riverside Avenue, Suite 200, Jacksonville, FL 32202.

Availability of Companion Documents

The following are available:

- Clinical practice guidelines for hypothyroidism in adults: cosponsored by the American Association of Clinical Endocrinologists and the American Thyroid Association. Supplementary data. 2012. 4 p. Available in Portable Document Format (PDF) from the American Association of Clinical Endocrinologists (AACE) Web site .
- American Association of Clinical Endocrinologists protocol for standardized production of clinical practice guidelines—2010 update. Endocrine Pract 2010;16:270-283. Electronic copies: Available in Portable Document Format (PDF) from the AACE Web site .

Print copies: Available from the American Association of Clinical Endocrinologists (AACE), 245 Riverside Avenue, Suite 200, Jacksonville, FL 32202.

Patient Resources

None available

NGC Status

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